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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/094,921	06/15/1998	HORST LINDHOFER	80309	9008

7590 08/26/2003

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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1642	26

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/094,921	Applicant(s) LINDHOFER ET AL.	
	Examiner Anne Holleran	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,13-21,23,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 13-21, 23, 26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed on April 30, 2003 is acknowledged.

2. Claims 1-8, 13-21, 23, 26 and 27 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

4. The rejection of claims 14, 17 and 18 under 35 U.S.C. 112, 2nd paragraph, is withdrawn in view of the amendment to the claims.

Claim Rejections Maintained:

5. The rejection of claims 1-8, 13, 15, 16, 19-21, 23, 26 and 27 under 35 U.S.C. 103(a) as being unpatentable over Volker et al (U.S.Patent 5,911,987; issued June 15, 1999; 102(e) date Feb. 21, 1997) in view of Deo et al (U.S. Patent 5,837,243; issued Nov. 17, 1998; filed June 7, 1996) and further in view of Lindhofer et al (Lindhofer, H. et al, J. Immunology, 155: 219-225, 1995) is maintained for the reasons of record.

Applicant's arguments have been carefully considered, but fail to persuade. The amendment of claim 1, changing the binding of the bispecific antibodies from "tumor antigen" to "tumor-associated" antigen fails to change the scope of the claims. The specification does not contain a definition of "tumor-associated" such that one would understand that the tumor antigen

is limited to endogenous tumor antigens. Applicant states that general usage of the term "tumor-associated" would lead one of skill in the art to understand that the claims require that the bispecific antibody bind to an endogenous tumor antigen. However, applicant provides nothing more than an opinion to support this contention. Because the specification fails to define the scope of "tumor-associated", and because claims must be interpreted with the broadest reasonable scope, and because once a tumor cell is infected with a virus and viral antigens are then presented on the surface of the infected tumor cells (an "association" with the tumor cell), applicant's arguments fail to persuade.

With regard to remainder of the argument, it appears that applicant is restating arguments offered in previous responses. Applicant argues that the prior art fails to suggest the claimed invention, and presents arguments by attacking each reference individually. Applicant argues that Volker fails to suggest the claimed invention, because antegenizing with a virus is a necessary step in the method of Volker, and that the present claims and specification do not suggest such a step. However, the scope of the claims does not exclude such a step. Applicant argues that the preferred embodiments of Deo are the use of antibody fragments that contain Fc portions, whereas the claimed invention is drawn to methods using intact antibodies. However, Deo is cited to demonstrate that usefulness of antibodies comprising Fc regions is known in the art. Applicant argues that because Lindhofer teaches a method of antibody purification that takes advantage of the heterologous nature of a rat/mouse bispecific antibody, and does not teach using such a bispecific antibody to arm tumor cells, that Lindhofer fails to teach the claimed invention. This argument is not found persuasive because the advantages that Lindhofer teach with respect to purification and high yield would have motivated one of skill in the art to use the antibodies of

Lindhofer. The reason for using a product taught in the prior art does not have to be the same as the reason presented in the specification. Thus, the prior art as a whole appears to teach the claimed inventions. Volker teaches arming tumor cells with antibodies that bind to an antigen present on tumor cells and to a T cell and Deo teaches arming tumor cells with antibodies that bind to a tumor antigen and to an Fc receptor. Thus, the combination of the references teaches one that arming tumor cells with antibodies that bind to both a T cell and to an Fc receptor would be useful for the treatment of cancer. Lindhofer teaches one of the specific examples of the bispecific antibodies and teaches advantages for using such a bispecific antibody.

New Grounds of Rejection:

6. Claims 1, 14, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volker (supra) in combination with Deo, in view of Honsik (U.S. Patent 4,844,893; published July 4, 1989) and further in view of Lindhofer (supra).

In view of the amendment to claim 14, claims 1, 14, 17 and 18 are interpreted as drawn to methods of making a vaccine preparation that comprises mixing tumor cells with a bispecific antibodies that bind to a T cells and to a tumor cell (and also comprising an Fc receptor) and further with peripheral blood mononuclear cells (claim 1 is included because it comprises steps a, b, c, and therefore may include additional steps, such as a step where peripheral blood mononuclear cells are added to the tumor cells).

The combination of Volker and Deo fails to teach making a vaccine preparation that comprises peripheral blood mononuclear cells. However, Honsik teaches arming peripheral blood mononuclear cells with antibodies that bind to an Fc receptor and to a tumor antigen (see

col. 4, line 55 – col. 5, line 9), and also the arming of target cells or T cells with bispecific antibodies that bind to a T cell and to a tumor antigen (col. 5, line 10 – line 22). Honsik teaches making a preparation comprising a mixture of tumor cells, bispecific antibodies and armed effector cells (peripheral blood mononuclear cells armed with antibodies the bind to a tumor antigen and to an Fc receptor; see col. 5, lines 23-28). Honsik is relied upon to teach a vaccine preparation (a target cell killing composition) that contains peripheral blood mononuclear cells that are brought into contact with tumor cells by the use of an antibody that binds both to an Fc receptor and a tumor cell. In addition, Honsik teaches that the combination of activated effector cells and T cells are needed in a preparation that will be useful for tumor cell cytotoxicity (col. 5, lines 46-52).

The difference between the teachings of Honsik and that of the claims is that Honsik uses two antibodies the bring together tumor cells with T cells and peripheral blood mononuclear cells, whereas the claimed methods are drawn to methods where one antibody molecule is used, where the antibody has three binding capabilities. When Volker, Deo and Honsik are combined, the prior art as a whole suggest that for effective killing of tumor cells, both T cells and effector cells must be activated, the claimed methods are therefore, suggest by the prior art.

The combination of Volker, Deo and Honsik fails to teach the combination isotype bispecific antibodies recited in the claims. However, Lindhofer teaches that rat/mouse combinations made using the quadroma technique result in a higher yield of functional bispecific antibodies and also teach that a rat/mouse combination isotype is easier to purify (see pages 219-221 and Figure 1). Thus, it would have been prima facie obvious to one of ordinary skill in the art to have combined the teachings of Volker, Deo and Honsik with that of Lindhofer to have

made the claimed invention. One would have been motivated to combine the teachings of Lindhofer with that of Volker, Deo and Honsik, because Lindhofer teaches the advantages of using rat/mouse combinations in purification of bispecific antibodies and in generating high yields of usable antibody product.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
August 22, 2003

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